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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/642,284	08/18/2003	Izumi Kumagai	4600-0106P	2450

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
01/15/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/642,284	KUMAGAI ET AL.	
	Examiner	Art Unit	
	ANNE L. HOLLERAN	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,22,24,25 and 27-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *24 and 28-32* is/are allowed.

6)☒ Claim(s) *21,22,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 9/22/2008 is acknowledged.

Claims 21, 22, 24, 25, and 27-32 are pending.

Applicants request rejoinder of claims 24, 25, 28 and 29.

Claims 21, 22, 24, 25 and 27-32 are examined on the merits.

Claim Rejections Withdrawn:

The rejection of claims 24, 25, 28 and 29 under 35 U.S.C. 103(a) as being unpatentable over Abstract 3P-214 (Asano, R., et al, 75th Annual Congress of The Japanese Biochemical Society, 74(8): August 25, 2002; cited in the IDS; English translation provided) in view of Adair (Adair, J. R. et al, Human Antibodies Hybridomas, 5: 41-47, 1994; cited in IDS), in view of Gill (Gill, G.N. et al., The Journal of Biological Chemistry, 259(12): 7755-7760, 1984) and further in view of Wu (Wu, H. et al., J. Mol. Biol., 294: 151-162, 1999) is withdrawn.

The declaration under 37 CFR 1.132 filed 9/22/2008 is sufficient to overcome the rejection of claims 24, 25 and 28 and 29 under 35 USC 103(a) based upon Abstract 3P-214 in view of Adair, Gill, and further in view of Wu.

New Grounds of Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 21, 22, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 25 and 27 are indefinite because the phrase "the cells having phagocytosis or cytotoxic activity" lacks antecedent basis.

Claim 21 is indefinite because it is drawn to a method for the production of the single-chain polypeptide according to claim 28, but claim 28 is drawn to diabody-type bispecific antibodies that comprise two single chains.

Claim 22 is indefinite because it recites a step of assembling the single chain polypeptides produced by the method of claim 28. However, claim 28 is not drawn to a method of producing single chain polypeptides.

The rejections of claims 21 and 22 under 35 USC 112, second paragraph would be overcome by the following amendment to the claims:

Canceling claim 21, and amending claim 22 as follows.

Claim 22. A method for the production of a diabody-type bispecific antibody, comprising [assembling the single-chain polypeptides produced by the method of claim 28 to form a diabody-type bispecific antibody] **culturing a host cell transformed with a nucleic acid encoding a first polypeptide of claim 28, culturing a host cell transformed with a nucleic acid encoding a second polypeptide of claim 28, expressing the nucleic acids, collecting the expressed first and second polypeptides, purifying the first and second polypeptides, and assembling the first and second polypeptides to form the diabody-type bispecific antibody of claim 28,** and separating and collecting the diabody-type antibody.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of increasing the production of cytokines by cells expressing CD3 and having phagocytosis or cytotoxic activity, does not reasonably provide enablement for increasing the production of any cells (specifically those that do not express CD3) having phagocytosis or cytotoxic activity. Additionally, the specification is not enabling for methods where the culture system contains tumor cells that express any EGF receptor, but is instead enabling for methods where the culture system contains tumor cells that express Her-1/ErbB1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

Claim 25 has the intended use of increasing the production of cytokines by cells having phagocytosis or cytotoxic activity. Claim 27 is drawn to a method for increasing the production of cytokines by cells having phagocytosis or cytotoxic activity comprising adding the diabody-

type bispecific antibody of claim 28 (which has a binding specificity for CD3 and for Her-1/ErbB1) to a culture system containing cells having phagocytosis or cytotoxic activity and tumor cells. Thus, the purpose of the method is to use the bispecific antibody to bring together in close proximity cells that express CD3 (usually cytotoxic T cells) and tumor cells that bind to Her-1/ErbB1 (For example, see Negri, D.R.M., et al, Br. J. Cancer, 72: 928-933, 1995; page 928, left to right column, bridging paragraph; cited in IDS). However, not all cells having phagocytosis or cytotoxic activity are cells that would bind to bispecific antibodies of claim 28, because not all cells having phagocytosis or cytotoxic activity express CD3. For example, granulocytes, which are cells with phagocytosis activity, do not express CD3 (see Hausmann, R., et al., Int. J. Legal Med., 112: 227-232, 1999, page 230, right column).

The specification defines the term "EGF receptors" to include Her-1/ErbB1, Her-2/ErbB2, Her-3/ErbB3 and Her-4/ErbB4 (se page 7, 2nd paragraph). However, the bispecific antibody of claim 28 has a binding specificity for Her-1/ErbB1, and not for all EGF receptors. Therefore, the specification is not enabling for methods comprising the incubation of tumor cells that do not express Her-1/ErbB1 in combination with the bispecific antibodies of claim 28, because such method would not result in increasing the production of cytokines by cells expressing having phagocytosis or cytotoxic activity.

In view of the above, one of skill in the art would not be enabled by the specification to make and use the method of claim 27 as broadly claimed with a reasonable expectation of success.

This rejection would be obviated by the following amendment of claims 25 and 27.

Claim 25. The pharmaceutical preparation according to Claim 24 for use in increasing the production of cytokines by [~~the~~] cells **expressing CD3, and** having phagocytosis or cytotoxic activity.

Claim 27. A method for increasing the production of cytokines by [~~the~~] cells **expressing CD3, and** having phagocytosis or cytotoxic activity, comprising adding the diabody-type bispecific antibody according to Claim 28 to a culture system containing the cells **expressing CD3, and** having phagocytosis or cytotoxic activity**,** and tumor cells expressing the human EGF [~~receptors~~] **receptor, HER-1/ErbB1**.

Conclusion

Claims 24, and 28-32 are allowed. Claims 21, 22, 25 and 27 are rejected.

In response to applicants' request for rejoinder and allowance, the examiner placed two telephone calls to Thomas J. Siepmann on December 17 and 23, but these telephone calls did not result in allowance of the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the

status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
January 7, 2009
/Alana M. Harris, Ph.D./
Primary Examiner, Art Unit 1643